Applicants: NALDINI et al.

Atty. Dkt. No. : 1130-PCT-US
Art Unit : 1636
Date of Office Commn. : 6/26/2009
Date of Response : 7/2/2009 USSN : 10/554,181 Filed : 12/02/ Examiner : Catherine Hibbert

Page : 3

AMENDMENTS TO THE CLAIMS

This listing of claims will replace all prior versions of claims in the application:

- 1. (Currently Amended) A bidirectional promoter for expression of at least two coding sequences in opposite direction in animal cells comprising 5' end to 3' end:
 - a) a first minimal promoter sequence derived from of cytomegalovirus (CMV) or mouse mammary tumor virus (MMTV) genomes;
 - b) a full efficient promoter sequence derived from of an animal gene comprising an enhancer region and a second minimal promoter sequence;

the promoter driving coordinate two sequences а transcription of said coding sequences in the opposite orientation.

2. (Canceled)

- 3. (Currently Amended) The bidirectional promoter according to 1 wherein the full efficient promoter sequence derives from animal gene is an ubiquitously expressed genes comprising the phosphoglycerate kinase or the ubiquitin gene.
- (Previously Presented) A bidirectional expression cassette 4. essentially comprising the bidirectional promoter according claim 1, convenient insertion sites positioned downstream to each promoter, and polyadenylation sites positioned downstream to each insertion site.
- 5. (Original) The bidirectional expression cassette according further comprising at claim 4 least one post-

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Page: 4

transcriptional regulatory element positioned upstream to one or each polyadenylation site.

6. (Previously Presented) The bidirectional expression cassette according to claim 4 further comprising at least one internal ribosome entry site (IRES) sequence to express three or more genes.

- 7. (Previously Presented) An expression construct containing the bidirectional promoter according to claim 1.
- 8. (Previously Presented) An expression construct containing the bidirectional expression cassette according to claim 4.
- 9. (Previously Presented) A gene transfer expression vector containing the expression construct according to claim 7 further comprising lentiviral or retroviral sequences.
- 10. (Currently Amended) A <u>method</u> Method for the delivery and expression of multiple genes in animal cells comprising the gene transfer expression vector according to claim 9.
- 11. (Currently Amended) The <u>method</u> according to claim 10 wherein animal cells are tissue animal cells ex vivo.
- 12. (Currently Amended) The <u>method Method</u> according to claim 11 wherein <u>the tissue animal cells are comprising</u> brain neurons.
- 13. (Currently Amended) A method Method for the coordinate expression of two exogeneous coding sequences into in an animal cell comprising the following steps:
 - a) cloning said coding sequences into the gene transfer expression vector according to claim 9, each coding

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: 10/554,181 : 1636 USSN Art Unit

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Page : 5

> sequence under the control of one of the two promoters of the bidirectional promoter;

- b) transforming animal cells by means of said vectors; and
- c) allowing the expression of the vector.
- 14. (Currently Amended) The Method method for the coordinate expression of two exogeneous coding sequences according to claim 10-13 wherein the animal cell is an human cell.
- 15. (Currently Amended) The Method method for the coordinate expression of two exogeneous coding sequences according to claim 14 wherein the human cell is a retransplantable human cell.
- 16. (Currently Amended) The Method method for the coordinate expression of two exogeneous coding sequences according to claim 15 wherein the retransplantable human cell is an hematopoietic cell.
- 17. (Currently Amended) A Method method for generating a transgenic non human organism comprising the step of transforming appropriate cells with an expression construct containing the bidirectional cassette according to claim 7.
- generating a 18. (Currently Amended) A Method method for transgenic non human organism comprising the step of transforming appropriate cells by means of the transfer expression vector according to claim 9.